# ON CLINICAL MEDICINE
## WITH NOTES FROM THE DIARY OF A PART-TIME RESEARCHER*

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I GREATLY appreciate the honor of having been selected to deliver the Pirquet Lecture this year. I am aware that I owe this privilege partly to the role I played in founding the Pirquet Society of Clinical Medicine and partly to my role in discovering mercurial diuresis half a century ago. Therefore, I want to take my cues for this address from these two roles and discuss two topics which are close to my heart: the future of clinical medicine and the contributions that a part-time clinical investigator can make to advances in medicine.

### CLINICAL MEDICINE, PAST AND FUTURE

Clinical medicine has been the leitmotiv of our society since its founding. Its name was chosen to express our intention to follow the tradition of clinical medicine which had flourished so brilliantly during the golden age of the Vienna Medical School.[1]

What do we mean when we speak of "clinical medicine"? By definition it is "bedside medicine" (derived from *kline*, the Greek word for bed). It is a concept of medicine that has as its source the observation of the patient, attention to his complaints, and examination by means of our senses, and it has as its purpose the diagnosis and the cure of his ills.

Clinical medicine has a venerable history. It was created 2,500 years ago by Hippocrates, the Father of Medicine; it flourished in ancient Greece and Rome but apparently lapsed into oblivion in the western world during the age of scholasticism. It was revived by revolutionary thinkers such as Boerhaave, Sydenham, Laënnec, and Skoda, who made it the dominant force in medicine in the 19th and early 20th centuries. But where does it stand today? Does it still have and should it rightly keep the exalted position that it used to command?

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## Clinical Medicine vs. Laboratory Medicine

Many concerned observers[2, 3] believe that medicine is at a crossroad because time-honored and valued concepts of medicine appear uprooted by the rapid advances of scientific techniques. These changes are regarded with anxiety by all those who see in them signs of an ever-increasing trend toward mechanization and the ultimate dehumanization of the practice of medicine.[4]

Is this threat real? Why could not cooperation of clinical and laboratory medicine work as fruitfully in medical practice as it has done in research? Why could the laboratory not continue to serve as a helpful partner instead of becoming the oracle of medical practice? Is there already a noticeable trend to substitute a battery of laboratory tests for sound and carefully weighed clinical judgment? I am afraid there is. And this trend is hastened by a number of factors which favor "laboratory medicine" over the clinical approach.

One of these factors is the need for saving time as the deluge of demands for medical care taxes the working schedule of every physician; another is the patients' waning respect for what they regard as "horse-and-buggy medicine"; a third factor is the undeniable scarcity of physicians who master the difficult art of clinical medicine.

The attempt by some physicians to save time by using laboratory tests as a shortcut in place of thorough history taking and physical examination is spurious. These methods of examination are indispensable not only for their intrinsic value but also because they establish the personal relation between the sick man and his doctor. This relation has no substitute, and it cannot be established in a hurry. An unhurried office visit in the best traditional style will serve to provide the desired rapport; usually it will also result in a working diagnosis. In this way the patient will be spared the days or weeks of waiting anxiously for the final word.

The restlessness of the patient who would rather have "a quick and foolproof cancer test" than submit to a lengthy interrogation can be overcome by making him feel that this is not a tedious routine but something pertinent to his particular problem. And the resentment against a time-consuming physical examination will vanish as soon as the patient becomes aware that due attention is paid to the apparent site or sites of his complaints. It is self-evident that in psychosomatic maladies,

which represent the reason for 40 to 80% of all office visits, careful examination is often more than half the treatment.

The most serious threat to the future of clinical medicine stems from the established fact that the practice of medicine is an *art* as much as a *science*.[3, 5]

There is no doubt that the eagerness of patients as well as of doctors to economize with their time and to turn for help to advances in technology runs counter to good medical practice. But the great trouble with clinical medicine at all times has been the simple fact that it can flourish only in the hands of good clinicians.

Why cannot every good student of medicine who is intent upon being a clinician become one? The scientific qualifications can certainly be acquired successfully, given the necessary intelligence, training, and perseverance. Medicine as an *art*, however, can be mastered only by the student with the talents of the artist, the "born clinician." As such he must possess not only the old master's power of keen observation, his memory, and his patience, but also an artist's intuition and imagination to let him create in his mind a harmonious, persuasive, and meaningful picture out of odd fragments of raw material. Without these abilities there can never be a true clinician.

No wonder, then, that not every medical man strives for the laurels of the artist-clinician, and it seems to me that the ranks of clinicians are depleted not only by the attraction of many gifted men to the glories of pure science, but also by the reluctance of others to embark on the difficult road toward mastery of clinical medicine.

From these remarks you may sense my concern that clinical medicine, and with it the role of the clinician, may be in for hard times, and that their golden age may have passed; but this does not mean that clinical medicine is dead. Just the reverse: with the infusion of new blood from the medical sciences a new clinical medicine is developing which promises a brilliant future under the leadership of the new clinician if he combines the qualities of the legendary "old clinician" with those of the modern human biologist.[5]

## Work of the Part-Time Researcher

If we leave this brief analysis of the trends and the future of clinical medicine in general, and turn to a discussion of the role of the clinician in research, especially that of the part-time worker, the question will

arise at once whether the work that he can perform in his own realm, in the hospital wards, in the outpatient clinic, and in private practice can be meaningful and productive. In this day and age can significant advances in medicine possibly be expected from any source other than highly trained teams of investigators collaborating in well-organized projects and equipped with the most advanced technical facilities? With your permission I shall try to answer these questions on the basis of personal experience.

My esteemed predecessors as Pirquet Lecturers have all been Nobel Laureates or scientists of similar international renown. Each could unfold to you the proud history of successful work aided by outstanding teams of investigators.[6] I make no attempt to compete with the accomplishments of these eminent scientists, but I thought it might be worthwhile and fitting to relate to you on this occasion the more modest but always enthusiastic and sometimes successful work of a life-long part-time clinical researcher.

Many far-reaching, even revolutionary advances in the sciences have had very humble beginnings.[2, 7, 8] Everyone here is aware of the way in which Roentgen detected the penetrating power of cathode tube rays, or how Semmelweis discovered the contagious character of puerperal sepsis. Serendipity has played an important role in these and other major discoveries, but this fact has too often been deliberately suppressed.[9]

## Serendipity

Serendipity, as you probably know, is a term which Horace Walpole coined after he had read the fairy tale of the travels of the three princes of Serendip,[10] who chanced unexpectedly upon novel things which they had not been in quest of but which became the starting point for amazing discoveries because of the inquisitiveness and sagacity of these young men. In short, serendipity is a way of making discoveries without planning them. It is obviously not a recognized method for scientific research and, as Rossman noted when writing on the advance of science and the role of serendipity in it, "scientists tend to cover up any part that serendipity may have played in their own work. They do it in order to create the image of logic and purposeful design in pursuing their scholarly goal, a pursuit in which there cannot be a place for accidents, errors or human foibles." Let us not forget,

however, that pure accident is only the first step in serendipity. Much more than this is needed to attain its royal rewards: the intuition to recognize the potentials of the accidental observation, never-ending curiosity, and the patience and courage to embark on an adventure of which the duration is unknown and the end not in sight.

The background of discoveries made through serendipity can be related without embarrassment and without any retouching or retrospective alterations. It should be told factually not only for the sake of historical truth, but, most of all, to encourage members of the profession, young and old, to participate in research with the means at their disposal and to accept a challenge wherever they encounter it. My reports will let you glance behind the stage on which the dramas and the comedies of serendipity are enacted. They may reveal some of the fascination, the joys and the troubles, the rewards and the disappointments encountered during research on a small scale but over a wide range. The chapters which I have selected from my diary deal only with subjects whose investigation had not been planned in advance. No wonder then that all of them must truthfully begin with: "as it happened."

## The Discovery of Mercurial Diuresis[11]

May I take you back 50 years to recount the curious events that led to the introduction of the mercurial diuretics: the discovery being commemorated this year.[8] We must remember that no effective diuretic agent existed at that time and that it was the common fate of patients in congestive heart failure, as the saying went, to "drown in their dropsy."

As it happened, an 18-year-old girl with congenital syphilis and protracted diarrhea, bed-ridden, emaciated, and dehydrated (not edematous) was admitted in October 1919 to the Wenckebach Clinic in Vienna where I worked as a third-year medical student and clinical clerk. I was told to order a mercury salicylate solution for the girl as antisyphilitic treatment and to administer one injection every other day. But I made a mistake in the way I wrote the prescription. The pharmacy, therefore, never delivered the solution. After waiting a week for it, I was only too glad to accept a professional sample of a currently advertised organic mercurial from a helpful physician visitor and to substitute it for the missing compound. The trade name of this drug was Novasurol. I duly recorded every injection on the bedside chart

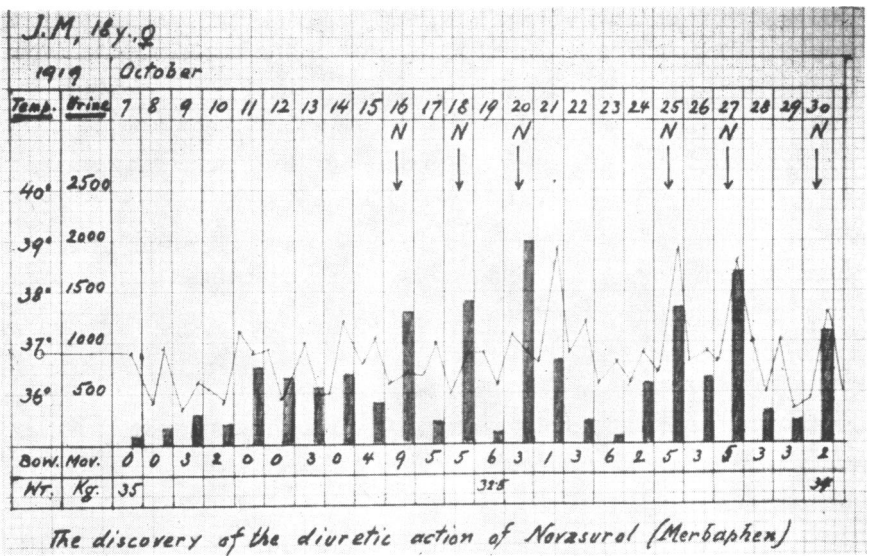



**Fig. 1. Bedside chart of the 18-year-old girl on whom the diuretic action of an organic mercurial preparation (Novasurol) was discovered. *N* indicates the day of the Novasurol injections; the dark columns show the daily volume of urine.**

on which the nurses also entered pulse, temperature and, in blue columns, the daily urine output (Figure 1). While marking each injection on the chart, I noticed that a tall blue column had appeared on the day of the first injection while previously these columns had been very low. The sudden rise in urinary volume was followed by just as precipitous a drop on the following day. These brief peaks repeated themselves on alternate days, the days of the Novasurol injections.

I reported these startling observations excitedly to my chief. To my disappointment I was informed that it was common knowledge that biological events ran in a wavelike rhythm, a law of nature which could well account for the ups and downs of our girl's urinary volume.

But I remained unconvinced and, being very young and not easily impressed by authority, I challenged this biologic law by simply omitting one ejection during a long weekend. During these days the output or urine remained very scanty again. But when, on Monday, the Novasurol injections were resumed, the flood of urine reappeared in a rhythmic cycle according to the days of injections.

This time I succeeded in getting the chief interested. Question after

question was discussed. What had happened? Was it really the mercurial that had produced the urinary floods? How did it do it? Perhaps by a fleeting antisyphilitic action on kidneys or on body tissues? And, if so, would it do the same in other syphilitic patients?

There was one patient in the ward, a middle-aged cab driver with syphilitic heart disease, who was totally water-logged in what was, by the then current criteria, terminal congestive failure. On my chief's order he was to receive the next Novasurol injection. Within 24 hours he voided more than 10 liters and we were sure that we had just witnessed "the greatest man-made diuresis in history." The next day the patient felt "like a new man," and he continued to live and work with the help of repeated injections of Novasurol for more than 10 years. After this first massive diuresis we still assumed that the effect was somehow related to the antisyphilitic action of mercury. But this belief was seriously shaken when other mercurial compounds failed to produce any diuretic effect in our syphilitic patients. So, with much trepidation, Novasurol was tried on a young boy with rheumatic heart disease in advanced congestive failure. To our delight, he, too, had a prompt and massive diuresis.

Now there was no more doubt that we had a new, powerful diuretic in our hands and that we were on the threshold of a new era for the cardiac patient.

All these exciting adventures took place within less than four weeks. We had been blessed with good luck. No severe allergic reactions and no mercurial poisoning occurred until the discovery was reported to the Society of Physicians in Vienna. Soon after this meeting, however, two patients died of acute hemorrhagic colitis. If such catastrophes had happened among our first cases it would, no doubt, have been the end of our experiments with Novasurol.

By the time the diuretic effect of Novasurol was first noted, it had been in use for seven years, and its antisyphilitic effectiveness had been reported in several publications, including a five-year study involving 900 patients who had received a total of 5,000 injections of this drug. It is hard to understand how the diuretic "side effects" could have escaped notice. I kept wondering about this until an older colleague told me why he had given up Novasurol in his treatment of venereal disease. So many of his patients had complained to him of having to urinate all the time and of getting terribly thirsty after their injections, that he had

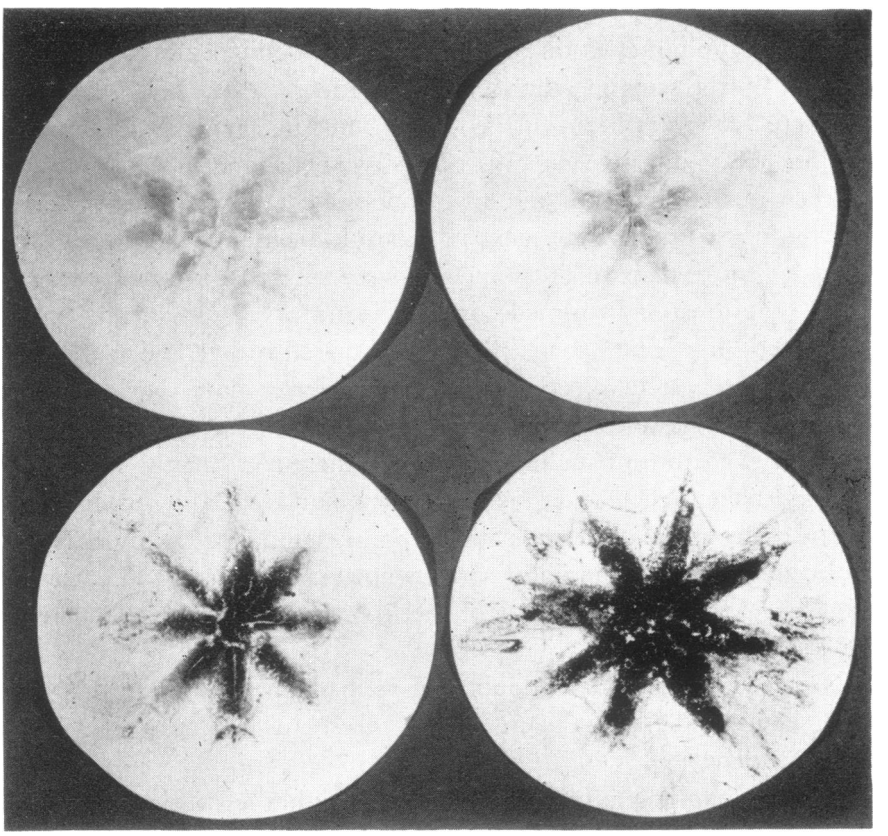


Fig. 2. Four paper filters with the dried plasma precipitated with trichloracetic acid showing the various shades (of green) indicating the bilirubin concentration in patients with different degrees of jaundice.

made up a standard reply to their gripes: "What's all the fuss about? Thank the Lord that you live in Vienna where there is a pub in every block and a comfort station at every street corner." Finally, however, he became tired of all these complaints and simply switched from Novasurol to a bismuth preparation. Thus the observation of the diuretic effect of Novasurol remained unreported for a few more years.

The mechanism of the diuretic action of Novasurol remained obscure for a long time. Many early attempts to elucidate it were all in vain. The time was not yet ripe for successful research in diuresis. Thus the use of mercurial diuretics had become standard therapy all over the

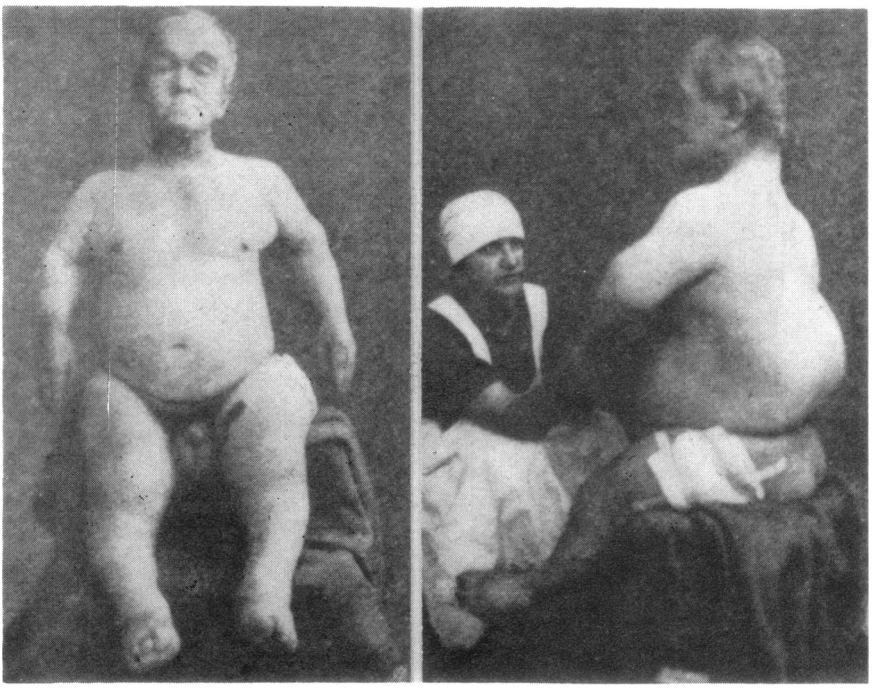


Fig. 3. Achondroplastic dwarf with a dorsolumbar gibbus and paraplegia. Reproduced by permission from: Donath, J. and Vogl, A. Untersuchungen über den chondrodystrophischen Zwergwuchs. *Wien. Arch. Inn. Med. 10*:1, 1925.

world long before advances in renal physiology could provide an understanding of the underlying principles.

## The Trichloracetic Acid Test for Hyperbilirubinemia

Another minor but rather useful contribution also had its origin in an accidental observation. As it happened, a series of paper filters, covered with serum protein precipitated by trichloracetic acid, had been left on the work bench in the laboratory and had dried there. I noticed that some of these precipitates had turned various tints of green while most of them remained colorless (Figure 2). The green precipitates were found to have come from blood specimens of patients who had frank jaundice or other disorders of the liver. On the basis of these observations, Berthold Zins and I devised a simple semiquantitative test for bilirubinemia, documenting the course of jaundice by using the filters as a permanent record.[12]

Fig. 4. Pre-Columbian figure of an achondroplastic dwarf with a dorsolumbar gibbus (the heavy cane suggests the possibility of paresis of the lower extremities).

A bit of new basic information also turned up while we were developing the new trichloracetic acid test. At low serum bilirubin levels the test was found positive in some patients but negative in others despite an identical icterus index. These findings suggested the subsequently proved existence of two different types of bilirubin in blood.

The trichloracetic acid test served its purpose well for about a decade when it was superseded by more convenient and exact quantitative methods.

## ACHONDROPLASIA[13]

*Gibbus formation.* My next story exemplifies a different road along which the part-time researcher can proceed from a problem encountered in his clinical work.

As it happened, an achondroplastic dwarf was admitted to our ward in 1924. He had a prominent dorsolumbar gibbus and was paralyzed from the waist down (Figure 3). The hunchback had been present since early childhood and was, according to the family, caused by a fall from the crib. The paraplegia, however, was recent.

The unusual kind of gibbus fascinated me and I began to look for achondroplastic dwarfs in the streets, in circuses, among Egyptian and pre-Columbian sculptures (Figures 4 and 5), among Renaissance paintings, and among illustrations in the older medical literature (Figure 6). It became apparent that exactly the same type of gibbus had been depicted in achondroplastic dwarfs often enough to refute the then current notion that the vertebral column was virtually unaffected by the basic disorder of the skeleton, and that a gibbus, when present, was incidental, caused by trauma or Pott's disease. Examination of achondroplastic skeletons in the Rokitansky anatomical museum showed that the spine was not spared and that of four achondroplastic skeletons one had a dorsolumbar gibbus (Figure 7). In achondroplastic babies, however, we could find no angular gibbus but only varying degrees of lumbar kyphosis (Figure 6). We therefore concluded that as soon as the child began to sit the weight of the trunk would increase the kyphosis and tend to convert the curved kyphosis into an angular gibbus (Figure 8). Based on this concept preventive orthopedic measures were devised which have in fact been able to protect achondroplastic children from developing this extreme deformity.

*Paraplegia.* The investigation of the paraplegia in our patient bore

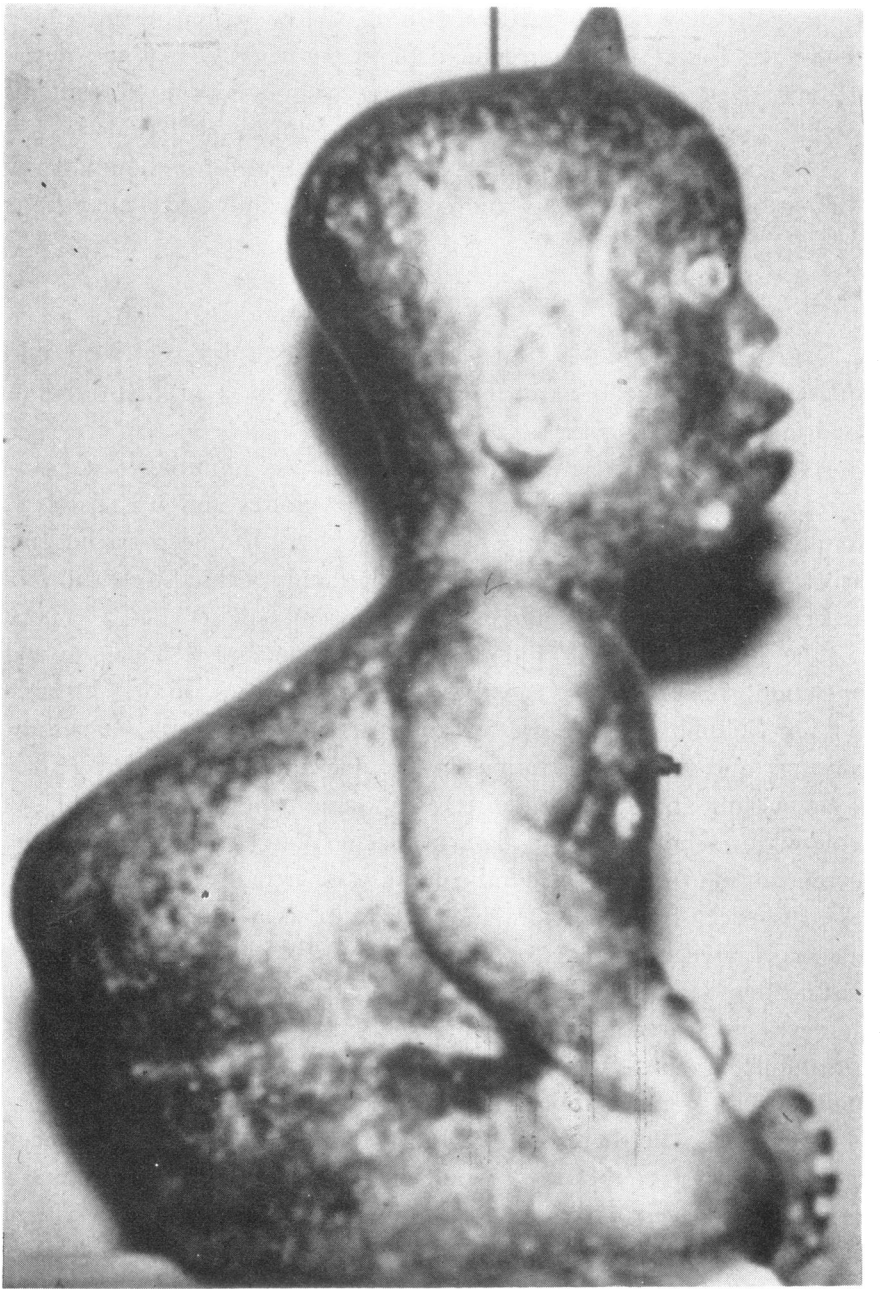


Fig. 5. Pre-Columbian figure of an achondroplastic boy with severe angular dorsolumbar gibbus.

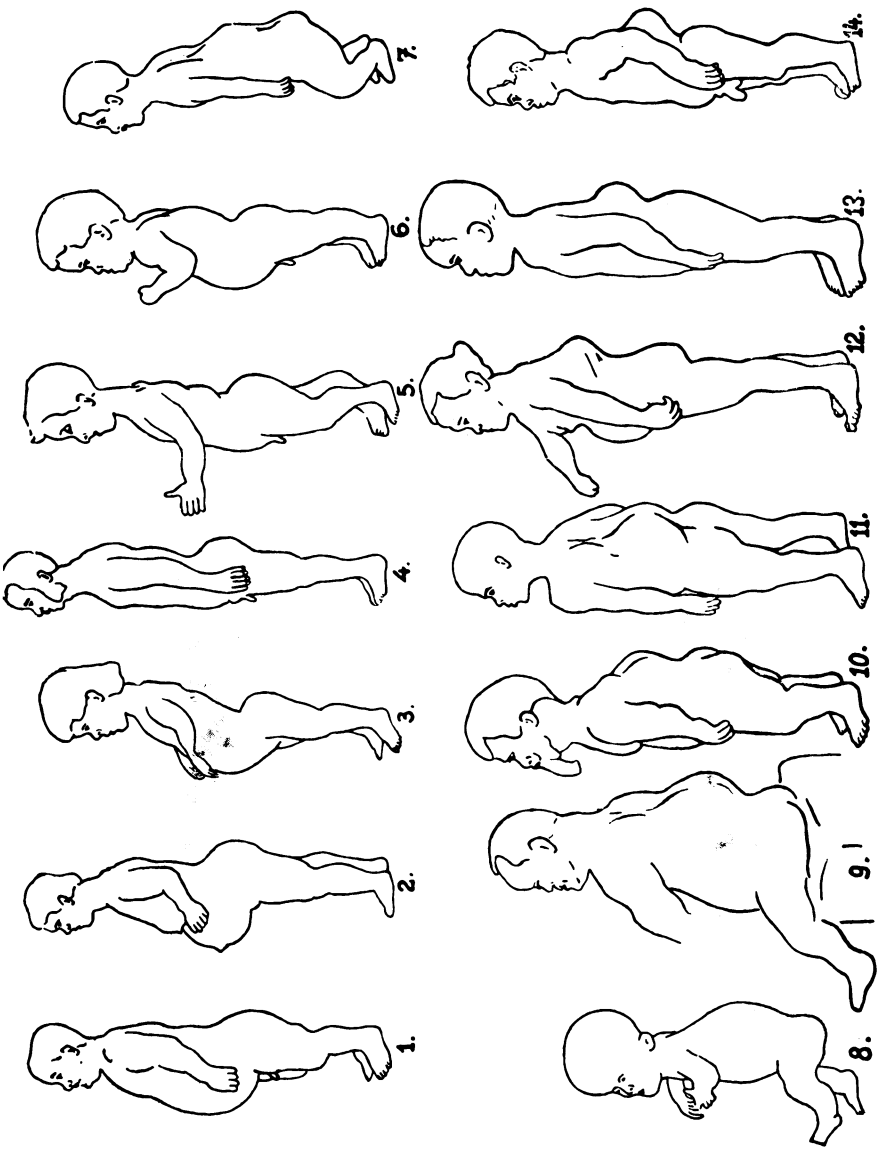



Fig. 6. Profile line drawings of achondroplastic dwarfts showing all degrees of changes of the spine, from the mildest to the most severe degrees of lumbar kyphosis. Note especially the young child (Number 8) with a curved kyphosis when just beginning to sit. Reproduced by permission from: Donath, J. and Vogl, A. Untersuchungen über den chondrodystrophischen Zwergwuchs. *Wien. Arch. Inn. Med. 10*:1, 1925.

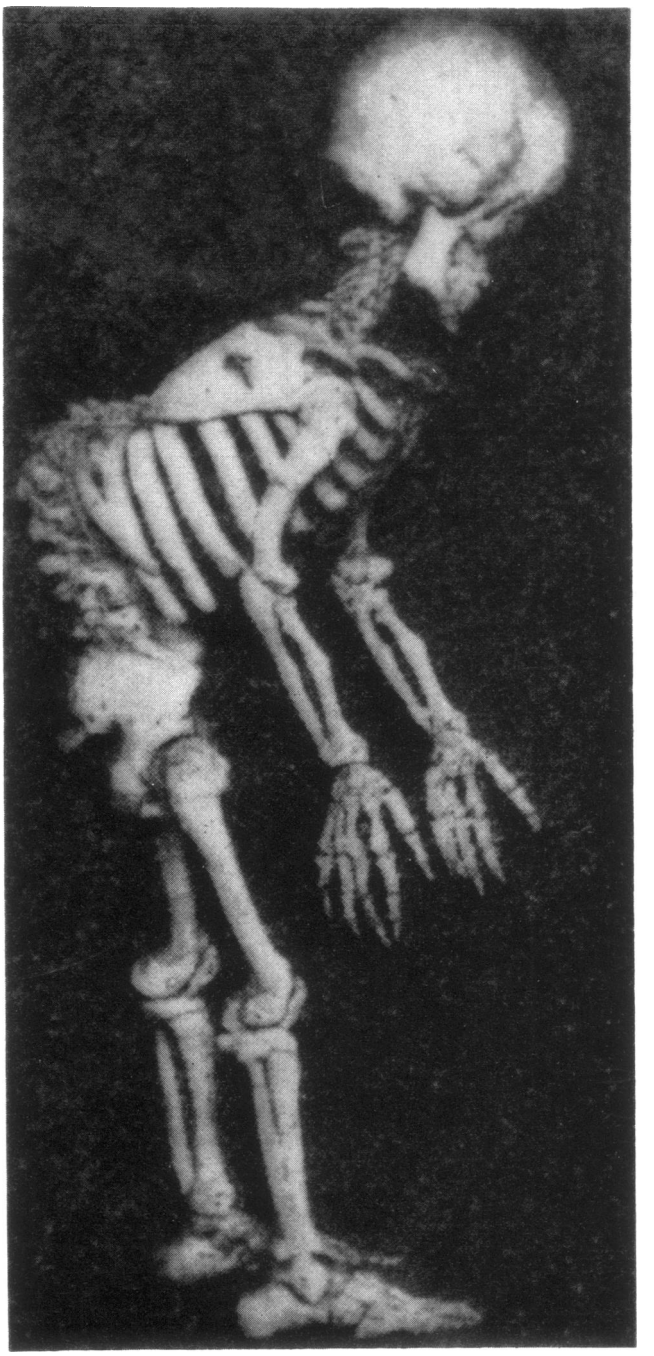


Fig. 7. Skeleton of an achondroplastic dwarf with a dorsolumbar gibbus with a wedge-shaped body of L 1 (forearms and hands of this 18th century specimen do not belong to this skeleton). From the Rokitansky Pathological Museum in Vienna. Reproduced by permission from: Donath, J. and Vogl, A. Untersuchungen über den chondrodystrophischen Zwergwuchs. *Wien. Arch. Inn. Med. 10*:1, 1925.

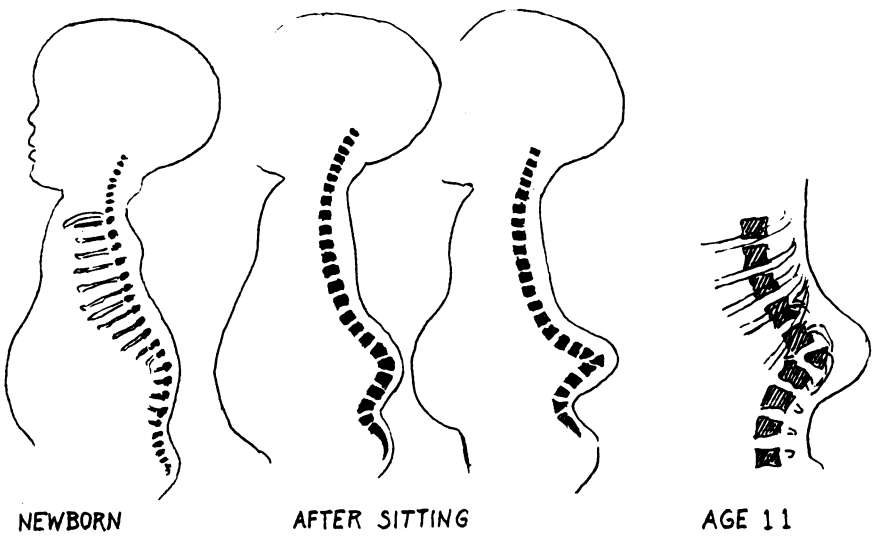



Fig. 8. Sketches indicating the development of an angular gibbus in an achondroplastic child born with a curved kyphosis. After the child begins to sit, the kyphosis increases, the keystone vertebra becomes wedge-shaped and finally dislocated posteriorly. This deformity can be prevented during this period by orthopedic measures.

even richer fruit; it succeeded in bringing about a significant change in the morbidity and mortality of achondroplastic dwarfs. The autopsy of our patient and measurements on the spine of achondroplastic skeletons revealed that the bony canal was just wide enough to fit a normal spinal cord tightly but with no room to spare (Figure 9). Since the spinal cord of an achondroplastic dwarf is normally developed, even minor disc protrusions or osteophytes will produce serious damage to the tightly encased nerve structures. For these reasons most achondroplastic dwarfs sooner or later suffer neurologic complications varying from herniated disc syndromes to complete paraplegia.

Under these circumstances we recommended freeing the cramped intraspinal structures by means of laminectomy. This procedure has now been carried out in many cases with gratifying results.

Through these observations achondroplasia has changed its place in medicine. In the past it had been regarded by the medical profession as the product of a caprice of nature but of no particular interest to any of the medical specialties except obstetrics. But since it has been shown than achondroplasia in itself can be the cause of serious illness and

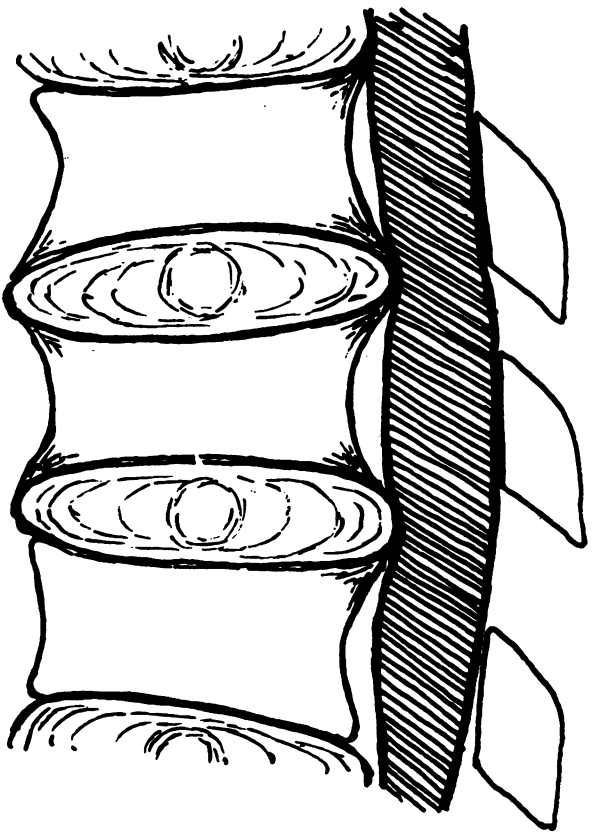
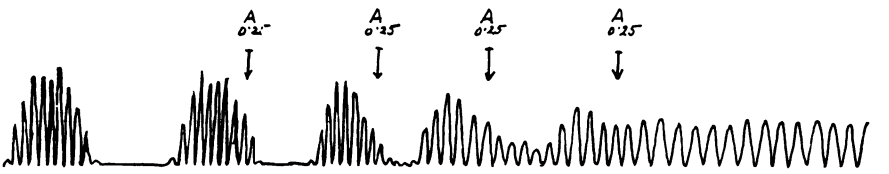


Fig. 9. Diagram indicating the disproportion between the achondroplastic spinal canal and the normally developed spinal cord. Minor osteophyte formations or disc herniations compromise the cord seriously.

death, pediatricians, orthopedists, and neurosurgeons have become aware of the problem and of the therapeutic possibilities. It has given me great satisfaction to have contributed to altering the grim fate of these otherwise healthy and often gifted persons.

## Cheyne-Stokes Respiration[14]

Cheyne-Stokes breathing became another target of my interest. Intermittent respiratory standstill has been known since antiquity as an ominous symptom of poisoning and of other serious disorders. No remedies existed. Sedation notoriously made the condition worse.




CHEYNE-STOKES RESPIRATION TREATED WITH AMINOPHYLLINE

Fig. 10. Diagram indicating the prompt excitatory effect of intravenously administered aminophylline upon the respiratory center, with abolition of the periodic respiration.

As it happened, one day I became a victim of this condition. After an operation in 1926, followed by large doses of morphine, my breathing became distressingly intermittent. Since the start of every period of hyperventilation produced quite some pain in the abdominal incision, I tried to figure out a way by which I could break the self-perpetuating cycle of Cheyne-Stokes breathing and thus avoid the need for the painful hyperventilation. I decided just to go on breathing voluntarily during the periods of respiratory standstill. However, the plan failed. I found myself incapable of using my respiratory muscles intentionally the moment the period of hyperventilation was over.

While recuperating I had time to think about how to abolish the vicious cycle of Cheyne-Stokes breathing, in other words, how to restore the responsiveness of the depressed respiratory center. I remembered then that on several occasions when, for diuretic purposes, I had injected aminophylline too fast by vein, the patient began to hyperventilate forcibly, to the point of dizziness and faintness. This observation indicated that aminophylline above a certain blood concentration may act as a potent respiratory stimulant and possibly be the drug for which I was looking.

Soon afterward I encountered a patient with severe Cheyne-Stokes respiration. He had pulmonary emphysema and had been given an injection of morphine for his air hunger. He was unresponsive and deeply cyanotic, and had periods of apnea. One fourth of an ampoule of aminophylline was injected rapidly by vein before each anticipated phase of respiratory standstill (Figure 10). Even before the entire ampoule was finished, normal respiration was restored and the patient was

fully alert. The action was equally rapid and effective in subsequent cases of Cheyne-Stokes breathing, whether caused by congestive heart failure, overdosage of sedatives, uremia, or brain tumor.

From these observations I had no doubt that aminophylline had a powerful direct stimulating effect on both the cerebral cortex and on the respiratory center. It took many years before the pharmacologists accepted the validity of this mechanism of action while the bedside observations had, to my mind, never permitted any other interpretation.

Aminophylline became and has remained the drug of choice for the symptomatic treatment of Cheyne-Stokes. Whenever insomnia is caused by periodic breathing, it is, in fact, the only effective "sleeping drug."

## Allergic Thrombocytopenic Purpura[15]

The last chapter selected from my diary for this paper deals with another exercise in serendipity. It goes back to the early 1930's when a veritable epidemic of a mysterious acute hemorrhagic disease swept through Europe. An ever-increasing number of people fell ill with what was considered fulminating Werlhof's disease. Petechiae and bruises appeared rapidly all over the body and bleeding occurred from nose, mouth, rectum, or bladder. This picture, alarming as it was, usually disappeared within a few days, but it was apt to reappear at any time. During these attacks complete or almost complete absence of blood platelets was found.

The public was frightened. The medical profession was puzzled. Treatment was haphazard because every treatment seemed effective for the moment: such as a variety of drugs, irradiation of the spleen and, in case of recurrence, splenectomy. But in at least one case bleeding occurred again after removal of the spleen as soon as the patient had returned home.

As it happened, I had a night emergency call to see an elderly man who had suddenly suffered a shaking chill, soon followed by the appearance of fresh bleeding spots all over the skin, blood-filled blebs on lips and tongue, oozing blood from mouth and nose, and gross hematuria. The absence of blood platelets confirmed the diagnosis of acute thrombocytopenic purpura. The following day the platelet count began to rise, all bleeding stopped and, after 3 days, the patient was well again.

Four weeks later I had to make another night emergency call to the same patient under the same circumstances. Thorough questioning, with

the help of the good memory of his housekeeper, revealed that the patient had on both these evenings taken a then popular somnifacient drug called Sedormid. The patient would never have suspected this drug as he had taken it in previous years regularly and with no ill effects.

I felt at that moment that I was on the track of the source of the current epidemic of bleeding. I promptly reached the patient I had seen previously after such episodes of bleeding, and others who, I knew, had suffered such attacks. And, indeed, all of them had taken Sedormid. Among them was the woman who, after being discharged following splenectomy, had suffered another severe attack of bleeding. She told me that, being a poor sleeper she had taken Sedormid frequently before and between her hospitalizations for hemorrhagic purpura. In the hospital, however, she was given some other sleeping pills, and recovered quickly from her hemorrhagic disease; but on returning home after her splenectomy she went back to her favorite Sedormid and promptly started to bleed again.

I was proud of my detective work and was convinced that I had found the key to the rash of bleeding disease and to its instant elimination. I felt that the facts should be made public without delay, preferably by the highest authority. So I hurried with my news to a leading hematologist, but received a cool and skeptical, almost hostile reception and, of course, no cooperation. I was confounded and at a loss to understand this attitude. Only much later I learned that the professor and his associate had just finished a major paper expounding a new theory on the cause of the epidemic and reporting the brilliant results they had obtained in treating the disease with a specially synthesized new drug.

When I just as naively approached the giant pharmaceutical company which produced Sedormid, in order to warn them of the dangers of their drug, I was in for another rude awakening. To my face I was politely admonished not to be hasty and not to let my imagination run away with me and, behind my back, I was accused of being a liar and publicity seeker who had talked patients into making false statements. When I insisted on publication of my findings and conclusions, I was threatened by the company with a suit for damages but at the same time was offered a considerable sum "for additional research" if I were only willing to postpone the publication of my findings for another year.

I realized then that I was on my own and had to face whatever criticism I might encounter in the forthcoming meeting of the Society

of Internal Medicine at which I was scheduled to present my observations in a paper titled "Allergic Thrombycytopenic Purpura."

Fortunately I had talked of my observations to another well-known hematologist. He rechecked the cases of purpura that had been admitted to his own service before. He confirmed the use of Sedormid among them and succeeded in opening the discussion on my paper before my adversaries had the opportunity to get up and annihilate me. Soon afterward the company put a warning label on the bottles and not much later withdrew Sedormid from the market.

It was thus established for the first time that in certain individuals a chemical compound would produce an allergic form of thrombocytopenic purpura. The mechanism was still obscure but because of the rapidity and completeness with which the platelets disappeared from the blood stream and then reappeared, I could not visualize depression or destruction of the megakaryocytes in the bone marrow as the cause. I surmised therefore that the circulating platelets must somehow be trapped in the periphery for the duration of the allergic reaction and must be released when it was over.

This hypothesis was essentially confirmed by later investigations that uncovered the complex immunologic mechanism involved.

In telling you these short stories, I followed the Roman dictum: *verba docent, exempla trahunt.* Words can teach but only examples can convince. It was my intention to convince you by these examples that major or minor contributions can be made by the means at everyone's disposal.

The history of my investigations clearly carries the marks of the advantages and the disadvantages that are inherent in part-time research. I have had the advantage of roaming freely in the wide field of medicine, of touching on many fascinating problems, of solving a few and, in other instances, of opening up a tiny window onto new vistas. These far-flung excursions have also broadened my experience as a clinician. The main disadvantage of not being a full-time investigator and a member of a team has been that I have had to leave my studies on completion of the clinical phase and let others work on the unresolved parts of the problems, from diuretics to allergic purpura.

However, I comfort myself with the realization that no research is ever finished, and that even trying to complete the research on all the

problems in which I was involved would have taken many busy lifetimes.

May I sum up the message I want to convey to you on this occasion?

Classical clinical medicine reached its culmination at the beginning of the 20th century. It had accomplished the transformation of Western medicine from an empirical and often irrational art of healing into a sound, sober, and well-organized system based on huge autopsy material. Since then the magnificent advances in biomedical sciences have created the miracle of modern medicine. These advances brought with them, by necessity, progressive specialization and fragmentation of medical practice and the tendency to treat diseases instead of human beings. In this manner the holistic approach of traditional medicine toward the sick is replaced by the pragmatic approach of providing expert knowledge and sophisticated techniques for the diagnosis and treatment of each of the patient's problems.

But must these two currents compete in modern medicine? Must the torrent of scientific progress engulf the gentler stream of clinical medicine, in which concern for the sick human being has always been the main motivation? Clinical medicine must dominate medical practice if it is not to become just another field of technology, alienating itself from the patient and losing his confidence. But how can clinical medicine survive the persistent onslaught from its Prometheuslike children, the medical sciences? How can it maintain its traditional role in the care of the patient?

Only by transforming itself into a new clinical medicine which must be a synthesis of benevolent interest and scientific accuracy, and of artistic intuition and scholarly prudence; in short, a synthesis of the ancient heritage of the art of healing and of wise utilization of the advances in medical science. In its forefront we shall find the new clinician, a human biologist with an incisive mind and an enthusiastic physician with imagination and compassion. The tasks of the new clinician will be titanic indeed.

If our medical schools succeed in producing physicians of this type—and the demand for them is overwhelming—then clinical medicine has a future worthy of its past and will be able to retain the role of leadership in medicine that seemed naturally to belong to it. To this end I have ventured, after 50 years in clinical medicine, to reemphasize its merits in the care of the sick, in the making of true physicians of

our students, and in providing an inexhaustible source for relevant research in medicine.

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